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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,187	08/20/2003	Allan Svendsen	4796.234-US	5703

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NOVOZYMES NORTH AMERICA, INC.
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NEW YORK, NY 10110

EXAMINER

SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/644,187

Applicant(s)

SVENDSEN ET AL.

Examiner

Tekchand Saidha

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-43 is/are pending in the application.
- 4a) Of the above claim(s) 40-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 24-28, 32 and 34-39 is/are rejected.
- 7) ☐ Claim(s) 29-31 and 33 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/182,859.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

Detailed Action

1. Applicants' preliminary amendment filed August 20, 2003, is acknowledged. As per the amendment claims 1-23 have been canceled. New claims 24-41 have been added, which are restricted as follows.
2. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 24-39, drawn to a variant of parent termamyl-like alpha-amylase variants (435/202) and detergent composition comprising the variants, and methods based thereof, classified in class 510, subclass 226.
 - II. Claims 40-43, drawn to DNA encoding alpha-amylase, vector, host cell, classified in class 435, subclass 252.3.
3. The inventions are distinct, each from the other because of the following reasons:

The DNA encoding the amylase of Group II and amylase of Group I are chemically and biologically distinct molecules. The enzyme and DNA have fundamentally different molecular structure, each with its own set of functionality. Enzyme, for example is biologically active, whereas DNA encoding the enzyme, is not. Additionally, the DNA constitutes the genetic material and is composed of the genes, and has other functions besides encoding the enzyme. Since the amylase (enzyme) and the DNA are biologically and chemically distinct, the manner of using the DNA may not necessarily involve the enzyme. At the minimum, the enzyme can be used to delineate molecular weight parameters in protein gel electrophoresis whereas the DNA can be used in hybridization protocols.

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4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Jason Garbell on May 2, 2004 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-39. Affirmation of this election must be made by applicant in replying to this Office action. Claims 4-43 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventor ship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventor ship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

7. When a non-provisional application claims the benefit under 35 USC 120 of a prior application, the first sentence of the specification should read, e.g., "This application is a continuation of U.S. Application No. 08/-----, filed -----, now US Patent. Applicants' continuation data is missing US Patent Numbers of 2 of the 3 the non-provisional application (continuation or divisional).

8. **Abstract**

*The abstract should be in narrative form and generally limited to a single paragraph within the range of 50 to 150 words [in length since the space provided for the abstract on the computer tape by the printer is limited]. The form and legal phraseology often used in patent claims, such as "means" and "said", should be

avoided in the abstract. The abstract should sufficiently describe the disclosure to assist readers in deciding whether there is a need for consulting the full patent text for details. MPEP 608.01(b).

The abstract needs to be amended by deleting the word 'said' on line 4, to avoid legal phraseology. Please make the change.

9. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

10. Claims 24-39 are pending and under consideration in this examination.

11. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 34 been renumbered 35.

12. Claims 24-27, 32, 34-39 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for Termamyl-like alpha amylase variants H405 or H406 of SEQ ID NO: 2 [*Bacillus licheniformis*]; and H406 of SEQ ID NO : 4 [*B. amyloliquefaciens*] and SEQ ID NO : 6 [*B. stearothermophilus*], and methods of use, does not reasonably provide enablement for Termamyl-like alpha amylase variants H405 or H406 in correspondence to SEQ ID NO: 2 from any source, including

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varying homologies of 80%, 85% & 90%. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 24-27, 32, 34-39 are so broad as to encompass any alpha-amylase variant wherein the sequence has been modified at positions H405 or H406 in correspondence to SEQ ID NO : 2, further having 80%, 85% & 90% identity to SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of alpha-amylases broadly encompassed by the claims. While Applicants clearly describe 3 species of *Bacillus* in making these mutational modifications and many *Bacillus* strains are well known in the art [see WO 95/26397, and the alpha-amylase described by Tsukamoto et al., Biochemical and Biophysical Research Communications, 151:(1988), pp. 25-31. (Applicants' specification page 3)]. It is also well known that the 3 disclosed *Bacillus* species share close amino acid sequence homologies. *B. licheniformis* alpha-amylase comprising the amino acid sequence shown SEQ ID NO:2 (commercially available as Termamyl™) has been found to be about 89% homologous with the *B. amyloliquefaciens* alpha-amylase comprising the amino acid sequence shown in SEQ ID No. 4 and about 79% homologous with the *B. stearothermophilus* alpha-amylase comprising the amino acid sequence shown in SEQ ID NO:6. However, such sequence homologies shared among species of *Bacillus*, is not universal as evidenced by the sequence search results of SEQ ID Nos. 2, 4 and 6, and therefore not shared by other species, plants, microorganism or animals, or where from the alpha-amylase hitherto

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remain uncharacterized. Further, there is no evidence of a corresponding histidine [or H] at position 405 or 406 of the alpha-amylase sequences across the breadth of the claim(s).

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of SEQ ID NO : 2, 4 & 6, and the prior art knowledge of the distinct regions of *Bacillus* alpha-amylase, as summarized on page 24 of the instant specification. Extrapolating to what is known of *Bacillus* amylases to amylases from any source is way beyond the instant disclosure.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple species and modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art has neither the guidance in the specification nor in the prior art to assume that such alpha-amylase mutants could be

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obtained from any source or from any *Bacillus* species (SEQ ID Nos. 2, 4, 6, etc.) wherein the amino acid sequence has already been modified to the extent of 10-20%.

The specification does not support the broad scope of the claims which encompass all modifications of any alpha-amylase or 10-20% modification of SEQ ID NOS: 2, 4 or 6, prior to subjecting the protein to further modifications at positions H405 or H406, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting alpha-amylase activity; (B) the general tolerance of alpha-amylase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any alpha-amylase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including alpha-amylase with an enormous number of amino acid modifications of any alpha-amylase from any source or from a sequence i.e. at least 80%, 85% or 90% homologous to the sequence of SEQ ID NOS: 2, 4 or 6. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of alpha-amylases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily,

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and improperly, extensive and undue in using the modified enzyme in the method claimed. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

13. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession Nos. A92389 [Takkinen et al. J. Biol. Chem. 258 : 1007-1013, 1983, see the enclosed sequence search alignment].

Takkinen et al. teach the amino acid sequence of an alpha-amylase having a sequence homology of about 82% compared to Applicant's SEQ ID NO : 2, and wherein position 406 has amino acid proline [P] instead of histidine [H]. The reference meets all the claim limitations, is therefore anticipatory.

14. Claims 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession Nos. P00692 [Takkinen et al., Biochem. J. 185 : 387-395, 1980, see the enclosed sequence search alignment].

Takkinen et al. teach the amino acid sequence of an alpha-amylase having a sequence homology of about 82% compared to Applicant's SEQ ID NO : 2, and wherein position 406 has amino acid proline [P] instead of histidine [H]. The reference meets all the claim limitations, is therefore anticipatory.

15. Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Accession Nos. P30921 [Kaneko et al., J. Gen. Microbiol. 135 : 3447-3457 (1989), see the enclosed sequence search alignment].

Kaneko et al. teach the amino acid sequence of an alpha-amylase having a sequence homology of about 11% compared to Applicant's SEQ ID NO : 6, and wherein position 406 has amino acid Asparagines [N] instead of histidine [H]. The reference meets all the claim limitations, is therefore anticipatory.

16. Claims 29-31 & 33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

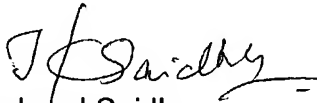
17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (571) 272-0940. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group in the Technology Center is 703 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 571 272-1600.



Tekchand Saidha

Primary Examiner, Art Unit 1652

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